Workshop 1: Best Practice Guidelines

Myeloma Guidelines Case Study

EURORDIS Membership Meeting
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Eric Low

On behalf of

Myeloma Patients Europe

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- Why they are important
- Case study
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What are clinical guidelines

- Clinical guidelines are systematically developed statements, based on a thorough evaluation of the evidence, to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances, across the entire clinical spectrum. (patinetsafetyfirst.ie)
- Clinical guidelines are recommendations by NICE on the appropriate treatment and care of people with specific diseases and conditions within the NHS. They are based on the best available evidence. While clinical guidelines help health professionals in their work, they do not replace their knowledge and skills (nice.org.uk)

Why they are important

- Consensus of expert opinion
- National minimum standard of care
- Equity of access and clinical practice
- Support clinicians who are not experts
- Identify evidence gaps – driver for research investment and prioritisation
- Healthcare resource planning – budget impact
- Benchmark for good/bad practice
- Help empower patients and provide confidence

Case Study

Situation analysis

- In 1997 myeloma was a relapsing and remitting cancer with a median survival of two to three years
- Increasing number of treatment options – most of which were very expensive
- Lack of consensus on best approach
- Heterogeneity in clinical practice and postcode prescribing
- Patients were losing out as a consequence
- The need for national clinical guidelines identified
- UK Myeloma Forum and Myeloma UK designated by the British Committee for Standards in Haematology to write guidelines

BCSH/UKMF Myeloma Guidelines

bjh guideline

Guidelines for the diagnosis and management of multiple myeloma 2011

Jennifer M. Bird,[1] Roger G. Owen,[2] Shirley D'Sa,[3] John A. Snowden,[4] Guy Pratt,[5] John Ashcroft,[2] Kwee Yong,[3] Gordon Cook,[2] Sylvia Feyler,[6] Faith Davies,[7] Gareth Morgan,[7] Jamie Cavenagh,[8] Eric Low[9] and Judith Behrens[10] on behalf of the Haemato-oncology Task Force of the British Committee for Standards in Haematology (BCSH) and UK Myeloma Forum

[1]Bristol Haematology and Oncology Centre, University Hospitals Bristol NHS Foundation Trust, Bristol, [2]Department of Haematology, Leeds Teaching Hospitals NHS Trust, Leeds, [3]Department of Haematology, University College Hospital, London, [4]Department of Haematology, Sheffield Teaching Hospitals NHS Trust, Sheffield, [5]Department of Haematology, Heart of England NHS Trust, Birmingham, [6]Department of Haematology, Calderdale and Huddersfield NHS Trust, Huddersfield, [7]Haemato-oncology Unit, Royal Marsden Hospital, London, [8]Department of Haematology, St. Bartholomew's Hospital, London, [9]Myeloma UK, Edinburgh, and [10]Department of Haematology, St Helier Hospital, Carshalton, Surrey, UK

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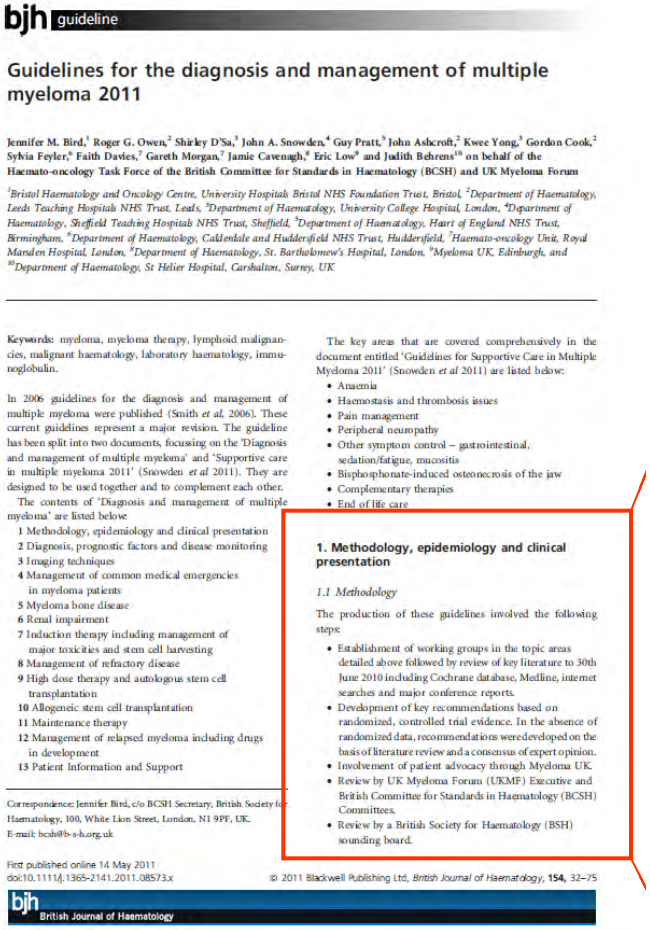
Methodology



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Keywords: myeloma, myeloma therapy, lymphoid malignancies, malignant haematology, laboratory haematology, immunoglobulin.

In 2006 guidelines for the diagnosis and management of multiple myeloma were published (Smith *et al*, 2006). These current guidelines represent a major revision. The guideline has been split into two documents, focussing on the 'Diagnosis and management of multiple myeloma' and 'Supportive care in multiple myeloma 2011' (Snowden *et al* 2011). They are designed to be used together and to complement each other.

The contents of 'Diagnosis and management of multiple myeloma' are listed below

1 Methodology, epidemiology and clinical presentation
2 Diagnosis, prognostic factors and disease monitoring
3 Imaging techniques
4 Management of common medical emergencies in myeloma patients
5 Myeloma bone disease
6 Renal impairment
7 Induction therapy including management of major toxicities and stem cell harvesting
8 Management of refractory disease
9 High dose therapy and autologous stem cell transplantation
10 Allogeneic stem cell transplantation
11 Maintenance therapy
12 Management of relapsed myeloma including drugs in development
13 Patient Information and Support

The key areas that are covered comprehensively in the document entitled 'Guidelines for Supportive Care in Multiple Myeloma 2011' (Snowden *et al* 2011) are listed below:

- Anaemia
- Haemostasis and thrombosis issues
- Pain management
- Peripheral neuropathy
- Other symptom control – gastrointestinal, sedation/fatigue, mucositis
- Bisphosphonate-induced osteonecrosis of the jaw
- Complementary therapies
- End of life care

1. Methodology, epidemiology and clinical presentation

1.1 Methodology

The production of these guidelines involved the following steps:

- Establishment of working groups in the topic areas detailed above followed by review of key literature to 30th June 2010 including Cochrane database, Medline, internet searches and major conference reports.
- Development of key recommendations based on randomized, controlled trial evidence. In the absence of randomized data, recommendations were developed on the basis of literature review and a consensus of expert opinion.
- Involvement of patient advocacy through Myeloma UK.
- Review by UK Myeloma Forum (UKMF) Executive and British Committee for Standards in Haematology (BCSH) Committees.
- Review by a British Society for Haematology (BSH) sounding board.

Correspondence: Jennifer Bird, c/o BCSH Secretary, British Society for Haematology, 100, White Lion Street, London, N1 9PF, UK.
E-mail: bcsh@b-s-h.org.uk

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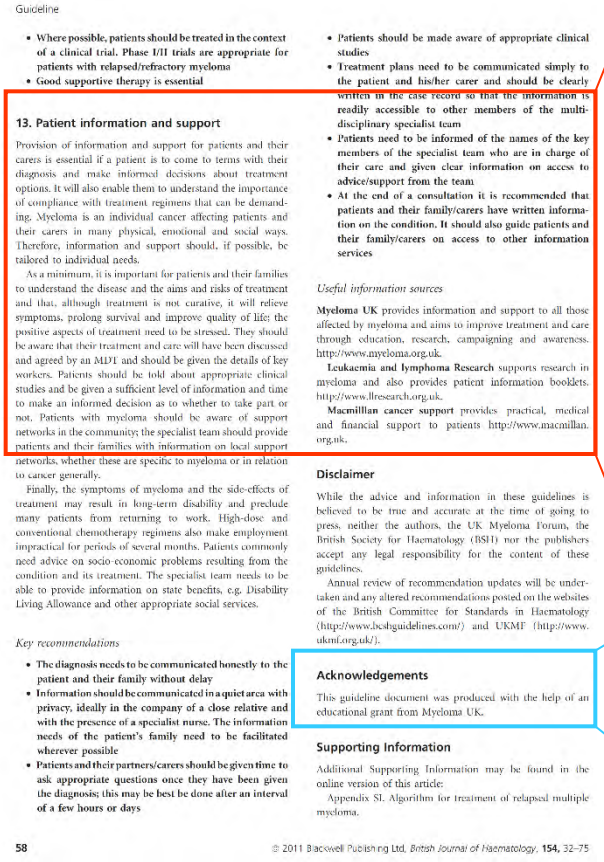
Patient Group Involvement



Guideline

- Where possible, patients should be treated in the context of a clinical trial. Phase I/II trials are appropriate for patients with relapsed/refractory myeloma
- Good supportive therapy is essential

13. Patient information and support

Provision of information and support for patients and their carers is essential if a patient is to come to terms with their diagnosis and make informed decisions about treatment options. It will also enable them to understand the importance of compliance with treatment regimens that can be demanding. Myeloma is an individual cancer affecting patients and their carers in many physical, emotional and social ways. Therefore, information and support should, if possible, be tailored to individual needs.

As a minimum, it is important for patients and their families to understand the disease and the aims and risks of treatment and that, although treatment is not curative, it will relieve symptoms, prolong survival and improve quality of life; the positive aspects of treatment need to be stressed. They should be aware that their treatment and care will have been discussed and agreed by an MDT and should be given the details of key workers. Patients should be told about appropriate clinical studies and be given a sufficient level of information and time to make an informed decision as to whether to take part or not. Patients with myeloma should be aware of support networks in the community; the specialist team should provide patients and their families with information on local support networks, whether these are specific to myeloma or in relation to cancer generally.

Finally, the symptoms of myeloma and the side-effects of treatment may result in long-term disability and preclude many patients from returning to work. High-dose and conventional chemotherapy regimens also make employment impractical for periods of several months. Patients commonly need advice on socio-economic problems resulting from the condition and its treatment. The specialist team needs to be able to provide information on state benefits, e.g. Disability Living Allowance and other appropriate social services.

Key recommendations

- The diagnosis needs to be communicated honestly to the patient and their family without delay
- Information should be communicated in a quiet area with privacy, ideally in the company of a close relative and with the presence of a specialist nurse. The information needs of the patient's family need to be facilitated wherever possible
- Patients and their partners/carers should be given time to ask appropriate questions once they have been given the diagnosis; this may be best be done after an interval of a few hours or days
- Patients should be made aware of appropriate clinical studies
- Treatment plans need to be communicated simply to the patient and his/her carer and should be clearly written in the case record so that the information is readily accessible to other members of the multidisciplinary specialist team
- Patients need to be informed of the names of the key members of the specialist team who are in charge of their care and given clear information on access to advice/support from the team
- At the end of a consultation it is recommended that patients and their family/carers have written information on the condition. It should also guide patients and their family/carers on access to other information services

Useful information sources

Myeloma UK provides information and support to all those affected by myeloma and aims to improve treatment and care through education, research, campaigning and awareness. http://www.myeloma.org.uk.

Leukaemia and lymphoma Research supports research in myeloma and also provides patient information booklets. http://www.llresearch.org.uk.

Macmillan cancer support provides practical, medical and financial support to patients http://www.macmillan.org.uk.

Disclaimer

While the advice and information in these guidelines is believed to be true and accurate at the time of going to press, neither the authors, the UK Myeloma Forum, the British Society for Haematology (BSH) nor the publishers accept any legal responsibility for the content of these guidelines.

Annual review of recommendation updates will be undertaken and any altered recommendations posted on the websites of the British Committee for Standards in Haematology (http://www.bcshguidelines.com/) and UKMF (http://www.ukmf.org.uk/).

Acknowledgements

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Algorithm for treatment of relapsed multiple myeloma.

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readily accessible to other members of the multidisciplinary specialist team

- **Patients need to be informed of the names of the key members of the specialist team who are in charge of their care and given clear information on access to advice/support from the team**
- **At the end of a consultation it is recommended that patients and their family/carers have written information on the condition. It should also guide patients and their family/carers on access to other information services**

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BCSH/UKMF Supportive Care Guidelines

bjh guideline

Guidelines for supportive care in multiple myeloma 2011

John A. Snowden,[1] Sam H. Ahmedzai,[2] John Ashcroft,[3] Shirley D'Sa,[4] Timothy Littlewood,[5] Eric Low,[6] Helen Lucraft,[7] Rhona Maclean,[1] Sylvia Feyler,[8] Guy Pratt[9] and Jennifer M. Bird[10] On behalf of the Haemato-oncology Task Force of the British Committee for Standards in Haematology and UK Myeloma Forum

[1]Department of Haematology, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, [2]Academic Unit of Supportive Care, The University of Sheffield, Sheffield, [3]Department of Haematology, Leeds Teaching Hospitals NHS Trust, Leeds, [4]Department of Haematology, University College Hospital, London, [5]Department of Haematology, John Radcliffe Hospital, Oxford, [6]Myeloma UK, Edinburgh, [7]Department of Clinical Oncology, Freeman Hospital, Newcastle, [8]Department of Haematology, Calderdale and Huddersfield NHS Trust, Huddersfield, [9]Department of Haematology, Heartlands Hospital, Birmingham, and [10]Avon Haematology Unit, Bristol Haematology and Oncology Centre, Bristol, UK

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Patient Group Involvement

Although much of the supportive care can be provided by the haematologists and their teams principally responsible for the care of patients with myeloma, if patients fail to respond or experience intolerable side-effects, advice should be sought from other specialist teams. In some patients, satisfactory symptomatic management is often only achieved through good multidisciplinary collaboration and specialist input from colleagues in Palliative Medicine, Pain Management, Clinical Oncology and Orthopaedics. This is probably best achieved through the routine multidisciplinary team (MDT) meetings (NICE, 2003a). Management of psychological aspects is also important. Outside of the hospital environment referral can be made to the community palliative care team or local hospice service.

These guidelines should be read in conjunction with the British Committee for Standards in Haematology (BCSH) Guidelines for Diagnosis and Management of Multiple Myeloma 2011 (Bird *et al*, 2011), which they complement. Management of symptoms in patients with myeloma at all stages should follow the principles of evidence-based palliative medicine, where possible. Where appropriate, levels of evidence are provided. As there was a view that many haematologists would welcome specific guidance in certain areas, certain therapeutic regimens have been suggested, most of which would be in the remit of haematological practice. In other areas, the guidelines make suggestions for specialist care outside of haematology. However, these guidelines should not be taken as prescriptive as variations exist. The guidance may not be appropriate to all patients and individual patient circumstances or clinician preferences may reasonably favour an alternative approach.

The draft guideline was produced by the writing group consisting of authors, assisted by other members of the broader BCSH Myeloma Guidelines group. Involvement of patient advocacy was achieved through Myeloma UK. The guidelines were subsequently revised by consensus by the UK Myeloma Forum Executive and members of the Haemato-Oncology Task Force of the BCSH. The guidelines were then reviewed by a sounding board of approximately 100 UK haematologists, the BCSH the British Society for Haematology Committee and the comments incorporated where appropriate. Criteria used to quote levels and grades of evidence where specified are as outlined in appendix 3 of the Procedure for Guidelines Commissioned by the BCSH (http://www.bcshguidelines.com/BCSH_PROCESS/42_EVIDENCE_LEVELS_AND_GRADES_OF_RECOMMENDATION.html) and US Agency for Healthcare Research and Quality (summarized in the Appendix I). In preparing these guidelines the authors have considered overall cost-effectiveness of recommended interventions as well as clinical efficacy data but formal health economic assessments have not been carried out.

The use of these guidelines to assist management of individual patients should be combined with appropriate professional training. All drug doses should be checked at reference sources, such as the British National Formulary (BNF), Palliative Care Formulary (PCF) or similar. The authors, BCSH or publishers cannot take legal responsibility for individual patient management.

2. Management of anaemia

Anaemia (haemoglobin concentration <120 g/l) is common in myeloma and is present in approximately 75% of patients at diagnosis (Kyle *et al*, 2003). In most patients the anaemia will be normochromic and normocytic and attributed to the myeloma itself and/or the myelosuppressive effect of the chemotherapy. Other causes, such as haematinic deficiency or bleeding, should be excluded. Fatigue is also reported by many patients and may be caused by both physical and psychological factors related to the disease and its treatment but anaemia has been shown to be an important contributory factor (Cella *et al*, 2004). A European wide survey in patients with myeloma suggested that prevalence of anaemia during chemotherapy is around 85% (Birgegard *et al*, 2006).

Anaemia may be managed by blood transfusion or treatment with erythropoiesis-stimulating agents (ESAs). Blood transfusion may be very helpful in the short-term correction of moderate to severe anaemia in a symptomatic individual. Minimally or asymptomatic individuals with mild or moderate anaemia (due to their disease) may be observed and some will become less anaemic as the myeloma is controlled with chemotherapy. ESA treatment is recommended for anaemic patients with myeloma with associated renal impairment (Locatelli *et al*, 2004). ESA doses of <20 000 iu/week may be adequate in patients where renal disease is the main cause of the anaemia. In the UK, it may be necessary to refer the patient to a renal physician to access NHS funding for ESAs.

Data from randomized trials, which have included patients with myeloma, suggest that ESAs increase the haemoglobin concentration in around two thirds of patients, reduce transfusion need and have a significant positive impact on quality of life (Littlewood *et al*, 2001; Osterborg *et al*, 2002; Hedenus *et al*, 2003).

Recent guidelines from the American Society of Haematology and American Society of Clinical Oncology recommend ESAs to be administered at the lowest dose possible and should increase the haemoglobin to the lowest concentration possible to avoid transfusions (Rizzo *et al*, 2010). European guidelines suggest consideration is given to initiating ESAs in symptomatic patients with a Hb of <110 g/l (Bokemeyer *et al*, 2007). In the UK, NICE has not recommended treatment for cancer-treatment related anaemia (except in ovarian cancer).

In patients undergoing high dose therapy, treatment with ESAs during the period of cytopenia has no impact on reducing transfusion need. In contrast, some studies with small numbers of patients suggest that starting ESA treatment on day +30 can increase haemoglobin concentration and reduce transfusion need after both autologous and allogeneic transplants (Baron *et al*, 2003; Vanstraelen *et al*, 2005).

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Dissemination and adoption

- Publication in peer reviewed journal (BJH)
- Implemented through regional cancer and local academic networks
- Patients given adoption flyers to take with them to hospital
- Presentations at regional, national and international meetings
- Used by several other countries
- Collaboration with Nordic Myeloma Study Group
- Feedback very positive but limited proactive evaluation

Limitations

- Guidelines not mandatory
- Often out of date by time published
- Evidence based and therefore only as good as available evidence
- Lack of evidence for every clinical situation – so gaps
- No cost effectiveness analysis
- Not predictive or algorithmic
- Often not linked to registries/outcome databases

Future

- Move towards predictive treatment algorithms (stratified medicine, diagnostics)
- Health economic evaluation
- Linked to registries/outcome databases
- Driver for identification, acceleration and adoption of innovation
- Better reflect payer concerns
- Built around patient values and preferences

Role of patient groups

- Call for their existence
- Patient involvement in their design
- Adoption, diffusion and uptake
- Monitoring and evaluation
- Myeloma Patients Europe Report on Myeloma Patient Perspectives

SUMMARY

- Important role in defining best practice and improving the treatment and care of patients with specific diseases
- Often not mandatory and limited
- Move towards predictive/costed pathways/algorithms
- Must involve patients